

Amendments to the Specification:

Please replace the original paper copy of the Sequence Listing with the amended substitute paper copy of the Sequence Listing filed herewith.

Replace paragraph [0038] at page 10 with the following amended paragraph:

FIGS. 1A-1B are ~~FIG. 1 is a photographic images image~~ of two northern blots probed with ³²P-labelled neublastin cDNA, comparing relative levels of expression of the neublastin gene in various human adult tissue types (panel A) and in various regions of the adult human brain (panel B).

Replace paragraph [0041] at page 10 with the following amended paragraph:

FIGS. 4A-4C are ~~FIG. 4 is a graphical illustrations illustration~~ of the effect of neublastin on the survival of cultured rat embryonic, dopaminergic, ventral mesencephalic neurons and ChAT activity in cholinergic cranial nerve motor neurons in serum-free medium. In particular, FIG. 4A is an illustration of the dose-response curve for recombinant GDNF on ChAT activity (dpm/hour). FIG. 4B is an illustration of ChAT activity (dpm/hour) using diluted conditioned medium from either neublastin producing or GDNF-producing cells. FIG. 4C is an illustration of the number of tyrosine hydroxylase immunoreactive cells per well.

Replace paragraph [0042] at page 11 with the following amended paragraph:

FIGS. 5A-5C are illustrations ~~FIG. 5 is an illustration~~ of the effect of neublastin secreted from HiB5pUbi1zNBN22 cells on the function and survival of slice cultures of pig embryonic dopaminergic ventral mesencephalic neurons co-cultured with either HiB5pUbi1zNBN22 cells (neublastin) or HiB5 cells (control). FIG. 5A and FIG. 5B illustrate dopamine released to the medium at DIV12 (Dopamine (pmol/ml) - day 12) and DIV21 (Dopamine (pmol/ml) - day 21), respectively. FIG. 5C is an illustration of the number of tyrosine hydroxylase immunoreactive cells per culture (TH-ir cells per culture) at DIV21.

Replace paragraph [0045] at page 11 with the following amended paragraph:

FIG. 8 is an illustration of neublastin specific primers used to identify the cDNA clone encoding the human neublastin polypeptide that hybridize to nucleic acids that encode neublastin polypeptides, but do not hybridize to nucleic acids encoding the other known GDNF family members (i.e., GDNF, Persephin and neurturin). The neublastin primers correspond to SEQ ID NO:17 (top strand) and SEQ ID NO:18 (bottom strand), the persephin primers correspond to SEQ ID NO:58 (top strand) and SEQ ID NO:59 (bottom strand), the neurturin primers correspond to SEQ ID NO:60 (top strand) and SEQ ID NO:61 (bottom strand), and the GDNF primers correspond to SEQ ID NO:62 (top strand) and SEQ ID NO:63 (bottom strand).

Replace paragraph [0051] at page 12 with the following amended paragraph:

FIG. 14 is a plasmid map of pET19b-Neublastin, along with the sequence of the synthetic gene for Neublastin. Both the DNA (SEQ ID NO:52), including the complimentary strand (SEQ ID NO:53), and translated protein (SEQ ID NO:54) are shown.

Replace paragraph [0052] at page 12 with the following amended paragraph:

FIG. 15 is a plasmid map of pMJB164-HisNeublastin, along with the sequence of the synthetic gene for HisNeublastin. Both the DNA (SEQ ID NO:55), including the complimentary strand (SEQ ID NO:56), and translated protein (SEQ ID NO:57) are shown.

Replace Table 3 at page 59 with the following amended table:

Table 3:

Amino Acid Sequence Comparison of Neublastin to Persephin, Neurturin, and GDNF

Neurturin-full (NO:49) -----MQRWKAALASVLCSSVLSIWMCREGLLLSHRLGPA
 Neublastin (NO:9) MELGLGGLSTLSHCWP RRQPALWPTLAALALLSSVAEASLG SAPRSPAPREGPPP
 Persephin-full (NO:50) -----
 GDNF_HUMAN-full (NO:51) -----MKLWDVVAVCLVLLHTASAFPLPAGKRPPEAPAEDRSLGRRRAPFALSSDS

Neurturin-full LVPLHRLPRTL DARIARLAQYRALLQGAPDAMELRELTWPAGRPPGPRRRAGPRRR
 Neublastin VLASPAHGLPGGRTARWC SGRARRPPPPQPSRPAPPPAPPSALPRGGRAARAGGPG
 Persephin-full -MAVGKFLGLSLLLLSLQLQGQGWGPDARGVPVADGEFSSEQVAKAGGTWLGT HRPL
 GDNF_HUMAN-full NMPEDYPDQFDDVMDFIQATIKRLKRSPDKQMAVLP RRERNRQAAAANPENS RGKG

Neurturin-full RARARLGARPCGLRELEVRVSELGLGYASDET VLF~~RY~~CAGACEA-AARVYDLGLRR
 Neublastin SRARAAGARGCRLRSQ LVPVRALGLGHRSD ELVR~~FR~~FCSGSCRR-ARSPHDSLAS
 Persephin-full ARLRRALSGPCQLWSLTLSVAELGLGYASEEKVI~~FR~~Y CAGSCPRGARTQHGLALAR
 GDNF_HUMAN-full RRGQRGKNRGCVLTAIHLNVTDLGLGYETKEELI~~FR~~YCSGSCDA-AETTYDKILKN

* * : * ****: . * : * *: *: * * * . *

Neurturin-full LRQRRRLRRE---RVRA~~Q~~PCCRPTAYEDEV SFLDAHSRYHTVHEL~~S~~ARECACV-
 Neublastin LLGAGALRPPPGSRPVS~~Q~~PCCRPTRYE-AVSFMDVNSTWRTVDRL~~S~~ATACGCLG
 Persephin-full LQQQGRAHGG-----~~P~~CCRPTRYT-DVAFLDDRHRWQRLPQL~~S~~AAACGCGG
 GDNF_HUMAN-full LSRNRRLVSD---KVG~~Q~~ACCRPIAFDDDL SFLDDNLVYHILRKH~~S~~AKRCGCI-

* . **** : : *: * . : : . ** *. *

* indicates positions which have a single, fully conserved residue.

: indicates that one of the following 'strong' groups is fully conserved:

-STA, NEQK (SEQ ID NO:64), NHQK (SEQ ID NO:65), NDEQ (SEQ ID NO:66),
 QHRK (SEQ ID NO:67), MILV (SEQ ID NO:68), MILF (SEQ ID NO:69), HY, FYW.

. indicates that one of the following 'weaker' groups is fully conserved:

-CSA, ATV, SAG, STNK (SEQ ID NO:70), STPA (SEQ ID NO:71), SGND (SEQ ID
 NO:72), SNDEQK (SEQ ID NO:73), NDEQHK (SEQ ID NO:74), NEQHRK (SEQ ID
 NO:75), HFY.

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Replace paragraph [0270] at page 60 with the following amended paragraph:

Based on this sequence alignment, neublastin was shown to be a member of the GDNF subfamily of neurotrophic factors (LGLG - FR(Y/F)CSGSC - QxCCRP - SAxxCGC (SEQ ID NO:76), the GDNF subfamily fingerprint, underlined in Table 3).